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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,764	TSUCHIYA ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9 and 12-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9 and 12-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 12/4/2007 is acknowledged. Claims 5-8 and 10-11 were cancelled. Claims 14-26 were added.

Claims 1-4, 9, and 12-26 are pending and examined on the merits.

Claim Rejections Withdrawn:

Claim Rejections - 35 USC § 102

2. The rejection of claims 1-7 under 35 U.S.C. 102(b) as being anticipated by Hansen (PNAS, 98(22): 12659-12664, 2001, Oct.; cited in the IDS) is withdrawn in view of the amendments to the claims.

3. The rejection of claims 10 and 11 under 35 U.S.C. 102(b) as being anticipated by Punt (Punt, C.J.A., et al. Cancer Immunol. Immunother., 38: 225-232, 1994; cited in the IDS) is withdrawn in view of the amendment canceling claims 10 and 11.

4. The rejection of claims 1-13 under 35 U.S.C. 103(a) as being unpatentable over Hansen (supra) in view of Larrick (Immunological Reviews, 130: 1992; cited in the IDS) is withdrawn in view of the amendments to the claims.

New Grounds of Rejection:

Claim Objections

5. Claim 22 is objected to because of the following informalities: misspelling of arteriosclerotic or atherosclerotic. Appropriate correction is required.

Claim Rejections – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the amendment adding claims 15 and 16 introduces new matter into the specification as originally filed.

Claims 15 and 16 are drawn to methods of claim 1, where the method is repeated for twenty or fewer B cells (15) or the method is repeated for five or fewer B cells.

The support pointed to by applicants is on page 6, lines 32-33. This passage does not provide support for the concept of repeating the method for specific numbers of cells. Instead the passage pointed to appears to be restricted to specifying the number of B cells within the sample to be analyzed. Therefore, the ranges of cell numbers recited in the claims, while mentioned in the specification, are not in the context of repeating the method, but in the context

of the sample size. Thus, the amendment adding claims 15 and 16, which are claims directed to repeating the methods, adds new matter to the specification as originally filed.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4, 17, 20, 21 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) as evidenced by Webster's New World™ Medical Dictionary (plasma cell. In Webster's New World™ Medical Dictionary, 2003. http://www.credoreference.com/entry/2438767).

Coronella teaches isolating human medullary ductal carcinoma (MC) surgical discard samples (constituting removal of the lesional tissue by surgical excision) and separating the plasma cells and lymphocytes from the cancer cells by Ficoll gradient centrifugation (see page 7890, 1st column). Single cells expressing CD38 ($CD38^{hi}$ cells) were sorted into wells of a 96-well PCR plate and amplified by RT-PCR to obtain λ Lc (lambda light chain), κ LC (kappa light chain) and γ1 Hc (gamma1 heavy chain) polynucleotides (page 7890, 2nd col.), which are sequences comprising variable regions of the light or heavy chains. Medulllary ductal carcinoma appears to be an inflammatory lesion (page 7889, 2nd col.). Webster's New World™ Medical Dictionary provides evidence that plasma cells are B cells, because the definition of a plasma cell is a "differentiated, mature lymphocyte in the B cell lineage".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-4, 14, 17-21 and 23 rejected under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with

evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June).

Coronella and evidentiary reference Webster's New World™ Medical Dictionary teach as set forth above.

Coronella fails to teach a method where the step of isolating a lesional tissue-infiltrating B cell comprises excising a region comprising the B cell from a section of the lesional tissue by laser microdissection (LMD).

However, a shown by the teachings of Obiakor, LMD is known in the prior art as useful for the collection of single B cells for the purpose of sequencing antibody VDJ polynucleotides. Obiakor teaches that tissues are frozen, stained and fixed (dehydrated) (see Table 1, page 56) and teaches that PCR may be used to obtain polynucleotides encoding antibodies.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Coronella to include an isolation step comprising LMD as taught by Obiakor. Obiakor also teaches that LCM method of isolating B cells allows the ability to visualize the collected samples prior to extraction and PCR reactions; that LCM easily collects 100 samples with 2 hours; and that LCM may emerge as the most user-friendly, reliable and consistent single cell collection system. Thus, the motivation to combine the references is provided by the teachings of Obiakor.

9. Claims 1-4, 9, 12, 17, 20, 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001,

November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Larrick (Immunological Reviews, 130: 1992; cited in the IDS).

Coronella and evidentiary reference Webster's New World™ Medical Dictionary teach as set forth above. Coronella also teaches that antibodies may be selected by panning libraries containing candidate antibodies against lesional tissue (see page 7891, 1st column).

Coronella fails to teach a method of producing an antibody comprising culturing a host cell and recovering the antibody.

Larrick teaches methods for making antibodies by isolating polynucleotides encoding antibody molecules and comprising the isolated polynucleotides into host cells for the production of antibody molecules. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Coronella with that of Larrick to produce and recover antibodies, and then to select antibodies that bound to lesional tissue. One would have been motivated by the teachings of Larrick that the method of cloning antibody encoding polynucleotides into host cells for the production of antibodies produces therapeutic antibodies.

10. Claims 1-4, 9, 12, 14, 17-21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), and further in view of Larrick (Immunological Reviews, 130: 1992; cited in the IDS).

Coronella and evidentiary reference Webster's New World™ Medical Dictionary teach in combination with Obiakor teach as set forth above. Coronella also teaches that antibodies may be selected by panning libraries containing candidate antibodies against lesional tissue (see page 7891, 1st column).

Coronella fails to teach a method of producing an antibody comprising culturing a host cell and recovering the antibody.

Larrick teaches methods for making antibodies by isolating polynucleotides encoding antibody molecules and comprising the isolated polynucleotides into host cells for the production of antibody molecules. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Coronella with that of Larrick to produce and recover antibodies, and then to select antibodies that bound to lesional tissue. One would have been motivated by the teachings of Larrick that the method of cloning antibody encoding polynucleotides into host cells for the production of antibodies produces therapeutic antibodies.

11. Claims 1-4, 14, 17-23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), and further in view of Koch (Koch, A. E. et al., American Journal of Pathology, 137 (5): 1199-1213, 1990).

Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June) teach as set forth above.

Coronella fails to teach a lesional tissue that is an atherosclerotic lesion, or an autoimmune disease lesion. However, the methods used in Coronella and Obiakor may be applied to atereriosclerotic lesions or autoimmune lesions such as the lesions of inflammatory abdominal aortic aneurysms, noninflammatory abdominal aortic aneurysms or occlusive aortas (page 1200, 1st column; see also abstract).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a lesion such as an arteriosclerotic lesion of the aorta or an inflammatory abdominal aneurysm to isolate B cells because Koch teaches that B cells are found in the adventia of pathologic tissues from inflammatory aneurysms, abdominal aortic aneurysms and occlusive aortas (see abstract), and because Koch suggests that the development of aneurismal disease may represent an immune-mediated event as a progression from occlusive disease to aneurismal disease (see page 1212 and abstract). The motivation for isolating B cells to make antibodies would be to discover the relevant antigens that may play a role in the pathogenesis of arteriosclerosis.

12. Claims 1-4, 14, 17-21, 23, 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of

Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), and further in view of Mallison (Mallison, S. M. et al., Infection and Immunity, 59(11): 4019-4025, 1991).

Coronella fails to teach a lesional tissue that is a lesion generated by an infectious pathogen, or an artificially prepared lesion. However, the methods used in Coronella and Obiakor may be applied to the study of such lesions, because Mallison shows that in models of periodontal lesions that there is an influx of B cells (antibody forming cells) where there is chronic inflammation; and that the influx of B cells is greatest for sites of chronic inflammation compared to sites with no inflammation or sites of acute inflammation (pages 4019-4024; see also abstract).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a lesion such as modeled periodontal lesions because Mallison teaches that B cells are found in sites with chronic inflammation even without the presence of antigen or activator. The motivation for isolating B cells to make antibodies would be to discover the relevant antigens that may play a role in periodontal disease and its associated inflammation.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
February 27, 2008

/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643